UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/516,294	09/12/2005	Susumu Muto	P26316	5597

7055 7590 09/19/2007

GREENBLUM & BERNSTEIN, P.L.C.
1950 ROLAND CLARKE PLACE
RESTON, VA 20191

EXAMINER
WEBB, WALTER E

ART UNIT	PAPER NUMBER
1609	

NOTIFICATION DATE	DELIVERY MODE
09/19/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

gbpatent@gbpatent.com
pto@gbpatent.com

Office Action Summary	Application No.	Applicant(s)	
	10/516,294	MUTO ET AL.	
	Examiner	Art Unit	
	Walter E. Webb	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/26/2006, 3/7/2006, 2/24/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

Claims 1-14 are pending and rejected.

Specification

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

Applicant's abstract exceeds 150 words and contains legal phraseology. Corrections should reflect the criteria above.

Applicant is reminded of the proper content of an Abstract of the Disclosure.

In chemical patent abstracts for compounds or compositions, the general nature of the compound or composition should be given as well as its use, *e.g.*, "The compounds are of the class of alkyl benzene sulfonyl ureas, useful as oral anti-diabetics." Exemplification of a species could be illustrative of members of the class. For processes, the type reaction, reagents and process conditions should be stated, generally illustrated by a single example unless variations are necessary.

Complete revision of the content of the abstract is required on a separate sheet.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating chronic rheumatism, does not reasonably provide enablement for preventing chronic rheumatism. The specification does not

enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In this regard, the application disclosure and claims have been compared per the factors indicated in the decision In re Wands, 8 USPQ2d 1400 (Fed. Cir., 1988) as to undue experimentation. The factors include:

1) the nature of the invention;

2) the breadth of the claims;

3) the predictability or unpredictability of the art;

4) the amount of direction or guidance presented;

5) the presence or absence of working examples;

6) the quantity of experimentation necessary;

7) the state of the prior art; and,

8) the relative skill of those skilled in the art.

The relevant factors are addressed below on the basis of comparison of the disclosure, the claims and the state of the prior art in the assessment of undue experimentation.

Factors 1 and 2: Applicant's invention is drawn to a medicament according to claim 1, which is used for preventive and/or therapeutic treatment of chronic rheumatism (claim 14).

Factors 3 and 7: In particular, one skilled in the art could not practice the presently claimed subject matter without undue experimentation because the artisan would not accept on its face that the prevention of chronic rheumatism, which exhibited

some sensitivity to the medicament of claim 1, could be effectively achieved by the administration of the claimed active agent. Based on the state of the art, as discussed below, the artisan would have only accepted that the treatment of chronic rheumatism could be achieved, rather than that such an agent could have been used to prevent chronic rheumatism.

As set forth in *In re Marzocchi* et al., 169 USPQ 367 (CCPA 1971):

"[A] [s]pecification disclosure which contains teaching of manner and process of making and using the invention in terms corresponding to the scope to those used in describing and defining subject matter sought to be patented must be taken as in compliance with the enabling requirement of first paragraph of 35 U.S.C. 112 unless there is reason to doubt the objective truth of statements contained therein which must be relied on for enabling support; assuming that sufficient reasons for such doubt exists, a rejection for failure to teach how to make and/or use will be proper on that basis, such a rejection can be overcome by suitable proofs indicating that teaching contained in the specification is truly enabling."

Factor 4: Applicant disclosed guidance in the form of inhibitory activity of the medicament of claim 1 against collagenous arthritis in a mouse. Applicant also disclosed how a human might be administered this composition. Still, further guidance is needed in regards to humans. To enable the Artisan to reasonably predict that Applicant's composition can prevent chronic rheumatism, Applicant should set forth a protocol or guidance as to how prevention of this disease could be achieved.

Applicant's disclosure is inadequate as to directing or guiding how the proposed agents can be employed to accomplish such objectives in a predictable manner.

Factor 5: While the present claims encompass preventing chronic rheumatism, Applicant's provide data evidencing a treatment, where a mouse was given a medicament of claim 1. See Applicant's specification at page 212 and corresponding figure 1 of Applicant's Drawings. No data has been provided, or reasonable scientific basis exists, for predicting a prevention of chronic rheumatism.

Treatment of Gout, a type of chronic rheumatism, for example, is well developed (see Gout: Crystal-induced Arthritides: Merck Manual Professional at http://merck.com/), but the state of the art with regard to preventing this disease in general is underdeveloped.

In this regard, The Merck Manuel is cited. In particular, there is no known agent that is effective against preventing Gout. The Merck Manuel reference clearly shows that for Gout, there is not one agent or combination thereof that is effective at preventing the precipitation of monosodium urate crystals into tissue and around joints, which is the cause of this disease (see Treatment at pp. 4-6).

Given that there was not known a specific agent or combination of agents effective to prevent Gout, one of ordinary skill in the art would not accept on its face Applicant's statement that such an objective could be achieved with any chronic rheumatism. The artisan would have required sufficient direction as to how to predict what particular forms of chronic rheumatism would actually show sensitivity to the presently claimed composition such that the artisan would have been imbued with at

least a reasonable expectation of success in preventing such diseases. Such success would not have been reasonably expected for preventing symptoms associated with the chronic rheumatism given the variable nature of treating Gout. The prevention of Gout, for example, would have been an outcome not reasonably expected by one of ordinary skill in the art. To the artisan, the concept of a single agent, or even a combination of agents, that is effective to prevent chronic rheumatism in a mammal would have been unique and, thus, met with a great deal of skepticism.

The Examiner acknowledges that the Office does not require the presence of working examples to be present in the disclosure of the invention (see MPEP §2164.02). However, in light of the state of the art, which recognizes the variable nature of treating Gout, there is no apparent disclosure to support the contention that chronic rheumatism can be prevented by simply administering, by any method, a medicament of claim 1, since the present specification fails to enable one of ordinary skill in the art to practice the entirety of the presently claimed invention.

Factor 6: The burden of preventing chronic rheumatism with the claimed composition is much greater than that of treating chronic rheumatism, with specific compounds of claim 1. Since the present specification would not enable the skilled artisan to prevent chronic rheumatism with the claimed composition, a clear burden of undue experimentation would be placed upon the skilled artisan in order to practice the full scope of the presently claimed invention.

Factor 8: In view of the discussion of each of the preceding seven factors, the level of skill in this art is high and is at least that of a medical doctor with several years of experience in the art.

Summary

As the discussion of the above 8 factors establish, practicing the claimed method in the manner disclosed by Applicant would not imbue one of ordinary skill with a reasonable expectation that preventing chronic rheumatism with the claimed composition could be achieved. In order to actually achieve such an objective, it is clear from the discussion above that one of ordinary skill could not rely on Applicant's disclosure as required by 35 U.S.C. § 112, first paragraph. Given that the art fails to recognize, and Applicant as failed to demonstrate, via direct evidence or sound reasoning, that chronic rheumatism can be prevented with the claimed composition, one of ordinary skill would be faced with the impermissible burden of undue experimentation in order to practice this embodiment of the claimed invention. Accordingly, claims 1-14 are deemed properly rejected.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29

USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-14 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-11 of copending Application No. 10516292 in view of Takeuchi et al., (WO 01/12588), English language equivalent EP 1219596. Claims 1-11 of the '292 application and 1-11 of the instant application contain the same limitations associated with formula I except the '292 application claims a medicament for prevention and/or treatment of cancers. Claims 12-14 of the instant application are obvious in view of WO 01/12588 since WO 01/12588 teaches the same medicament with those further limitations at pg. 2 ¶ [0006] and pg. 13 ¶ [0034].

Claims 1-14 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-25 of copending Application No. 10515622 in view of Takeuchi et al., (WO 01/12588), English language equivalent EP 1219596. Claims 1-25 of the '622 application and 1-11 of the instant application contain the same limitations associated with formula I. Claims 12-14 of the instant application are obvious in view of WO 01/12588 since WO 01/12588

teaches the same medicament with those further limitations at pg. 2 ¶ [0006] and pg. 13 ¶ [0034] of EP 1219596.

These are both provisional obviousness-type double patenting rejections.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Takeuchi et al., (WO 01/12588), English language equivalent EP 1219596.

Applicant's invention is drawn to a medicament having inhibitory activity against NF-kB activation, which comprises as an active ingredient a substance selected from the group consisting of a compound represented by the following general formula (I) and a pharmacologically acceptable salt thereof, and a hydrate thereof and a solvate thereof. (claim 1-14) The medicament is also an inhibitor against the expression of a gene for one or more substances from group δ, where the substance can be tumor necrosis factor (TNF), ICAM-1, VCAM-1 etc. (claim 12) or inflammatory cytokine (claim 13). The medicament also is used for preventive and/or therapeutic treatment of chronic rheumatism (claim 14).

Takeuchi et al. teach a compound of formula (I) with the limitations of claims 1-11 at page 2 lines 45-56, page 3 lines 1-55, page 4 lines 1-55, page 5 lines 1-56, page 6 lines 1-56, page 7 lines 1-55, page 8 lines 1-34. Takeuchi et al. teach that the compounds are effective in inhibiting the activation of NF-kB and useful anti-inflammatory agents, and immunosuppressive agents, as per claims 1 and 13. Takeuchi et al. teach that by inhibiting the activation of NF-kB the compound also inhibits the expression of TNF, ICAM-1, VCAM-1 etc. as per claim 12. (See page 2 ¶ [0006].). Takeuchi et al. also disclose an experiment where the compound was used to treat chronic articular rheumatism in a mouse, as per claim 14. (See page 13 at ¶ [0034].) The compounds disclosed by Takeuchi are weakly acidic substances and can be salt form with organic bases such as quaternary ammonium (see page 13 ¶ [0036]). The compounds and salts thereof can be prepared for oral or parenteral administration (see page 13 ¶ [0037-0041]).

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Walter E. Webb whose telephone number is (571) 270-3287. The examiner can normally be reached on 9:00am-5:00pm Mon-Fri EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

WW

JEFFREY STUCKER
SUPERVISORY PATENT EXAMINER